

This brief description of the work involved in preparing beach intelligence has indicated some of the problems that had to be overcome. The problems, of course, varied in degree with the amount and the reliability of the source data available. Beach intelligence, when prepared at a point far removed from operations, is still to some extent an art and not a science.

In addition to preparing beach intelligence reports, there was conducted laboratory experimental work which had direct bearing on the war effort. These experiments covered such items as the determination of depths over offshore bars or other bottom discontinuities and the characteristics of waves approaching a beach.

Other agencies were aided by wave tank experiments to determine the effects of storms and wave forces on pontoons or sunken ships designed as artificial harbors. Figs. 2 and 3 show before and after views of one of the test runs of storm waves on sunken model Liberty ships. In these experiments, an attempt was made to determine the best method of aligning the sunken ships to withstand wave forces. These tests were confirmed by experience during the Normandy invasion.

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#### BIOCHEMISTRY.—*The significance of tomatin in plant and animal disease.*<sup>1</sup>

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The elucidation of the biochemical nature of disease resistance in plants is a subject of challenging interest and one that is engaging the attention of this and other laboratories. Nearly all plants are prey to certain bacterial, fungal, or virus diseases. In many cases such diseases are responsible for major crop failures, which result in economic losses to the farmer, reduction in the supply of farm produce, and, ultimately, in increased costs to the consumer. For these reasons, plant-disease control has long been a problem of paramount importance to the agricultural scientist. Great progress in plant-disease control has been made through the development and application of bactericidal and fungicidal chemicals and through improvements in general farm practice. High in importance in minimizing the inroads of disease in plants has been the development, through intensive plant-breeding experiments, of varieties of economically important plants that are highly resistant to specific disease-causing organisms. By such means it has been possible to develop, in the case of many plants, varieties that will grow and produce in spite of infection (1, 2). As a result of these ex-

periments the plant geneticist can now provide plant-disease investigators with, for example, two tomato plants that will appear almost identical as to foliage and as to quality and size of fruit when grown in clean soil. However, when these plants are grown side by side in soil that is infested with the fungus *Fusarium oxysporum* f. *lycopersici*, one will wilt and die while the other will remain vigorous and produce fruit. One of these tomato plants is able to resist infection by *Fusarium* and survive, while the other is not able to resist the infection and succumbs. What is it then, in the chemical make-up of the plant that survives infection that is responsible for its resistance to wilt disease? This is the question for which it is hoped a reasonable answer can be found. It is believed that a full understanding of the chemical factors involved in conferring resistance upon a specific plant (the tomato) toward a specific disease organism (*Fusarium*) may provide clues upon which new and perhaps better methods for controlling disease in the tomato plant can be based. It is possible, further, that the knowledge gained in the biochemical study of disease resistance in the tomato plant may reveal factors of general significance to aid in the elucidation of the disease resistance mechanism of other plants to other pathogens.

<sup>1</sup> Received April 24, 1947. See footnote 1 of preceding article.

Investigations were initiated in this laboratory on the basis of a simple working hypothesis, namely, that certain tomato varieties are resistant to *Fusarium* wilt because they are able to produce an antibiotic agent or agents in sufficient quantity to inhibit the growth of the invading fungus. Early in the work partial substantiation of this hypothesis was obtained (3). It was found that the resistant tomato plant does elaborate a substance that markedly inhibits the growth of *Fusarium in vitro*, that the substance could be concentrated by suitable fractionation procedures, and that it satisfied the prerequisites of an antibiotic agent. This antibiotic agent from the tomato plant is now designated tomatin.<sup>2</sup>

During the past two years intensive efforts have been made to explore as fully as possible the many interesting lines of investigation that the discovery of tomatin has suggested. Research has been directed with four main objectives in view: (a) to isolate tomatin in the pure state and, once this is accomplished, to characterize it chemically; (b) to determine the antibiotic spectrum of tomatin, that is, to determine which microorganisms it inhibits and which it does not; (c) to ascertain the role, if any, played by tomatin in protecting tomato

plants against *Fusarium* wilt; (d) to investigate the possible occurrence of tomatin or tomatin-like substances in other plants. Much of this program still remains to be accomplished, but substantial progress has been made toward the achievement of each of the four objectives. It is known that tomatin is a water and alcohol soluble, remarkably heat stable, organic compound of relatively low molecular weight (3, 5); that it inhibits many other organisms besides *Fusarium*, among them bacteria, other fungi and yeastlike forms (5, 6); that tomatin or similar substances occur in plants like the potato, sweet potato, cabbage, and pepper but are absent from a majority of the other plants that have been examined (5); and finally that tomatin occurs in wilt-susceptible as well as in wilt-resistant tomato plants but probably to a greater extent in the latter (3, 7).

The discovery that tomatin is present in wilt-susceptible tomato plants was somewhat disappointing since, obviously, it would have been most attractive to be able to explain the susceptibility of certain tomato plants to wilt on the basis of the complete absence of tomatin from such susceptible varieties. Since this is not the case, attention was turned to the investigation of the effect of infection by *Fusarium* on the tomatin level in resistant and susceptible tomato plants. In these experiments it was found on the one hand, that a high level of tomatin is maintained in resistant tomato plants able to survive even though they are badly infected; on the other hand, it was found that tomatin gradually disappears from susceptible plants as invasion by *Fusarium* proceeds and that tomatin is completely absent from wilted and dying plants.

From these results it has been concluded tentatively that wilt-resistance or wilt-susceptibility in the tomato plant does not necessarily depend upon the presence or absence of tomatin, but rather upon the rate at which the plant is able to elaborate tomatin as the need for this protective substance arises. If the metabolic processes of a given tomato variety are capable of producing tomatin at a rate sufficient to

<sup>2</sup> The difficulty that has been experienced in selecting a suitable, unique name for this antibiotic agent demonstrates the pitfalls that confront those who would attempt to coin distinctive names for unidentified substances of biological origin. The substance was first named "lycopersicin," a term derived from *Lycopersicon*, the genus to which the tomato plant belongs. It was soon learned, however, that the term lycopersicin had been used previously to designate the red pigment of the tomato (4), and, although the use of the term in this sense was abandoned immediately owing to the more general acceptance of the term lycopene, it was considered wise, nevertheless, to abandon its use as a designation for the antibiotic agent from the tomato plant in order to avoid any possible confusion. After much deliberation the antibiotic was renamed "tomatin," derived simply from the name tomato. Very recently it has been learned that the term tomatin has also been used previously to designate an alcoholic beverage of foreign manufacture. In this instance, however, there seems to be little likelihood of confusion, and it is anticipated that the term tomatin will be retained to designate the antibiotic agent until its eventual isolation and identification may make it preferable to rename it in accordance with accepted chemical nomenclature.



maintain a protective level in the plant, then that variety will be resistant to wilt; if an adequate rate of tomatin production can not be maintained, the variety will be susceptible to wilt. While this conclusion is plausible in the light of the data, conclusive proof of its validity has not yet been obtained. It is known that wilting is accompanied by a disappearance of tomatin, but it can not be ascertained on the basis of the information now available whether tomatin disappears because the plant wilts or the plant wilts because tomatin disappears. The answer to this question, and an investigation of the mechanism whereby tomatin is produced by the plant, are among the more interesting problems for future investigation.

As has been mentioned, the antibiotic effectiveness of tomatin is not confined to the fungus *Fusarium*. It does, in fact, inhibit much more strongly cultures of certain of the fungi that cause disease in humans; among the organisms inhibited are those responsible for the dermatophytic infections such as ringworm and athlete's foot, and the more serious, often systemic infections such as blastomycosis, coccidioidomycosis, and histoplasmosis (5, 6) (Tables 1 and 2). To many this is perhaps the most interesting aspect of the work on tomatin, since a fungistatic agent suitable for parenteral use in humans is sorely needed by the medical profession. This is understandable, since no successful therapy exists at present for either the mild local infections or the serious systemic fungus infections in man. Tomatin is by no means the only antibiotic agent that possesses marked fungistatic properties, but those that have been tested heretofore are of limited clinical usefulness because of their toxicity (8). Accordingly, vigorous efforts are being made to ascertain the potentialities of tomatin for the treatment of fungus diseases in humans. The knowledge that tomatin inhibits these pathogenic fungi in culture represents only the first step in such an investigation. To be useful for human therapy tomatin must be shown to be of sufficiently low toxicity to permit safe administration or application in man

and to be effective against these same fungi in man. Whether tomatin possesses desirable properties in this regard is now being determined in cooperative experiments with the Duke University School of Medicine. These experiments have not yet progressed to the point where definite conclusions regarding the toxicity or *in vivo* effectiveness of tomatin can be drawn.

All the lines of research mentioned earlier in this report are being prosecuted as actively as possible. However, in all this work, and in plans for the future extension of these investigations, the isolation of tomatin in the pure state and its identification are of first importance. It is for this reason that the major current effort is being expended in this direction. Once tomatin has been obtained pure and its chemical nature are known it is probable that many of the present uncertainties regarding its possible role in the disease resistance mechanism of tomato plants and its possible effect upon the human organism can be clarified in direct, uncomplicated experiments.

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TABLE 1.—ORGANISMS WHOSE GROWTH IS COMPLETELY INHIBITED BY THE PRESENCE OF 1 UNIT TOMATIN PER ML. OF CULTURE MEDIUM

Organism	Disease and remarks
<i>Candida (Monilia) albicans</i> . . .	Moniliasis (thrush, bronchomycosis).
<i>Cryptococcus neoformans</i> } . . . . .	Cryptococcosis (European blastomycosis, torulosis).
<i>Debaryomyces histolytica</i> }	
<i>Trichophyton mentagrophytes</i> }	The dermatomycoses (ringworm, athlete's foot, etc.).
<i>Trichophyton interdigitale</i>	
<i>Trichophyton rubrum</i>	
<i>Trichophyton gypsum</i>	
<i>Epidermophyton floccosum</i>	
<i>Microsporum audouini</i>	
<i>Achorion gypsum</i>	
<i>Achorion schoenleinii</i>	
<i>Blastomyces dermatitidis</i> . . . . .	North American blastomycosis.
<i>Coccidioides immitis</i> . . . . .	Coccidioidomycosis.
<i>Histoplasma capsulatum</i> . . . . .	Histoplasmosis.

TABLE 2.—ORGANISMS WHOSE GROWTH IS PARTIALLY INHIBITED BY THE PRESENCE OF 1 UNIT TOMATIN PER ML. OF CULTURE MEDIUM

Organism	Disease and remarks
<i>Fusarium oxysporum f. lycopersici</i> . . . . .	Tomato wilt.
<i>Fusarium oxysporum f. pisi</i> . . . . .	Pea wilt.
<i>Fusarium oxysporum f. conglutinans</i>	Cabbage yellows.
<i>Fusarium oxysporum f. lini</i> . . . . .	Flax wilt.
<i>Actinomyces scabies</i> . . . . .	Potato scab.
<i>Sporotrichum schenckii</i> . . . . .	Sporotrichosis.
<i>Monosporium apiospermum</i> . . . . .	Maduromycosis (Madura foot, mycetoma)
<i>Aspergillus niger</i> } . . . . .	Rarely pathogenic.
<i>Aspergillus clavatus</i> }	
<i>Penicillium notatum</i> }	
<i>Staphylococcus aureus</i> . . . . .	Gram positive.
<i>Bacillus cereus</i> . . . . .	Gram positive.
<i>Bacillus mycoides</i> . . . . .	Gram positive.
<i>Bacillus subtilis</i> . . . . .	Gram positive.
<i>Escherichia coli</i> . . . . .	Gram negative.

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BIOPHYSICS.—*Harmony among vital substances*.<sup>1</sup> LUIS FELIPE VEGAS, Ministry of Public Works, Caracas, Venezuela. (Communicated by ALEXANDER WETMORE.)

As vital substances we here consider those, such as water, blood, etc., which are indispensable to the existence of man and the majority of living things. We have also placed under this heading those substances which are produced by a living organism, such as the aqueous and vitreous humors of the eye, or those of significance in the digestive process as saliva and hydrochloric acid. Finally, we have included those which are important in the conservation of species, as milk, etc.

From the chemical point of view, it is very difficult to establish a relationship of similarity between these substances. This is clearly seen in the case of hydrochloric

acid and albumen, in that the simplicity of the former (HCl) is in striking contrast to the complex form of the latter, which, according to A. Gautier, is: C<sup>250</sup> H<sup>409</sup> N<sup>67</sup> O<sup>81</sup> S<sup>3</sup>.

If we take into consideration the physical properties of these substances, we notice that they have certain similarities, since many are liquid at ordinary temperature, and all, in conformity with the latest theories, may have similar electronic arrangements. However, the similarity we shall discuss is a new aspect of the close relationship that exists between these substances. In 1937, we published a paper entitled *A study of the relations which exist between specific inductive capacity, the index of refraction of light, and density*.<sup>2</sup> In that

<sup>1</sup> Revised from the author's article *La armonía entre las sustancias vitales*, Bol. Soc. Venezolana Cienc. Nat. 9 (59): 163-166. 1944. Translated from the Spanish by Pedro J. Baldó and Armando Lazzari. Received February 5, 1946.

<sup>2</sup> Revista Colegio Ingenieros Venezuela 14 (123): 133-144. 1937.